REMARKS

Applicants and their counsel first thank Examiner Laura Schuberg and Examiner Blain Lankford for their courtesy of conducting an Examiner Interview with them on September 10, 2008.

Summary of the Examiner Interview

Applicants and their counsel discuss with Examiner Laura Schuberg and Examiner Blain Lankford about the pending claims, the prior art of record, and the differences between the present invention and the prior art of record. The Office Action dated April 14, 2008 and the discussions during the Examiner Interview have been carefully considered and the foregoing amendments have been made in response thereto.

In view of the foregoing amendments and the following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims.

Status of Claims

Claim 40 has been amended to replace the term "extracellular matrix" with "a musculoskeletal tissue" and recite that the at least one aldehyde group reacts with the musculoskeletal tissue to covalently bind the musculoskeletal tissue and the priming agent. Claim 40 has also been amended to incorporate the subject matter of claims 44 and 45 which have been deleted to avoid redundancy. Furthermore, claims 42 and 46 have been amended to be consistent with amended claim 40. Claims 50 to 59 have been canceled without prejudice and new claims 60 and 61 have been added. Canceled claims will be pursued in related patent applications.

Support for the above amendments can be found throughout the disclosure as filed originally. Specific support can be found at least in the originally filed application as provided in the following table:

Claim Elements	*Exemplary Support*
Claims 40 and 60: ...musculoskeletal tissue... ...the musculoskeletal tissue is a bone or	Page 2, paragraph [0005]; Page 8, paragraph [0043]; and Page 20, paragraph [0083].

Claim Elements	*Exemplary Support*
cartilage tissue…	
Claim 40: …the surface of a musculoskeletal tissue…	Page 7, paragraph [0038]; Figure 3; and Example I – page 22, paragraph [0093] to page 24, paragraph [0097].
Claim 40: …the at least one aldehyde group reacts with the musculoskeletal tissue to covalently bind the musculoskeletal tissue and the priming agent…	Page 37, Abstract (the last sentence); Figure 7; Page 5, paragraph [0025]; Page 6, paragraph [0034]; and Page 14, paragraph [0063].
Claim 40: …the first and second free radical polymerizable groups are each independently selected from the group consisting of an acrylate, diacrylate, oligoacrylate, methacrylate, dimethacrylate, and oligo methacrylate.	Page 3, paragraph [0018]; Pages 5 to 6, paragraph [0027]; Page 15, paragraph [0065]; Page 31, paragraph [00121]; and Example III – pages 27, paragraph [00108] to page 28, paragraph [00110].
Claim 40: …between the first and second free radical polymerizable groups…	Page 14, paragraph [0063] to page 16, paragraph [0068]; and Figure 7.
Claim 61: …ultraviolet radiation…	Original claim 11; and Page 3, paragraph [0017]; Page 4, paragraph [0019]; Page 6, paragraph [0028]; Page 15, paragraph [0064]; and Page 31, paragraph [00123].

Thus, no prohibited new matter is introduced into the original disclosure. Upon entry of these amendments, claims 40, 42, 43, 46 to 49, 60 and 61 remain be pending.

Summary of the Office Action

1. Claims 50 to 59 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claims 51 to 59 are rejected under 35 U.S.C. § 101 as allegedly not falling into a single statutory class of invention.

3. Claims 40 to 42, 44 to 52, and 54 to 59 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,624,245 to Wallace et al. (hereinafter "Wallace et al.") in view of Roberto Benson, Nuclear Instruments and Methods in Physics Research, 2002, B 191, 752-757 (hereinafter "Benson").

4. Claims 43 and 53 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Wallace et al. and Benson further in view of Hai et al., Bioconjugate Chem., 2000, 11, 705-713 (hereinafter "Hai et al.")

5. Claims 40 to 59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 40 to 75 of copending Application No. 11/369,578.

6. Claims 40 to 42, 45 to 48, 50 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 2, 9, 10, and 15 of copending Application No. 10/962,278 in view of Hai et al.

7. Claims 40 to 42, 45 to 48, 50 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 4 to 7, 18, 22, and 23 of copending Application No. 11/637,516 in view of Hai et al.

8. Claims 40 to 42, 45 to 47, 49 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 53, 63, 65, 77, and 86 of copending Application No. 10/681,753 in view of Hai et al.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claims 50 to 59 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

To expedite prosecution of the present application and without conceding to the merits of the rejections, claims 50 to 59 have been canceled. Applicants respectfully submit that the amendment has rendered the rejections under 35 U.S.C. § 112, second paragraph, moot.

Claim Rejections under 35 U.S.C. § 101

Claims 51 to 59 are rejected under 35 U.S.C. § 101 as allegedly not falling into a single statutory class of invention.

To expedite prosecution of the present application and without conceding to the merits of the rejections, claims 51 to 59 have been canceled. Applicants respectfully submit that the amendment has rendered the rejections under 35 U.S.C. § 101 moot.

Rejections under 35 U.S.C. § 103(a)

Claims 40 to 42, 44 to 52, and 54 to 59 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,624,245 to Wallace et al. (hereinafter "Wallace et al.") in view of Roberto Benson, Nuclear Instruments and Methods in Physics Research, 2002, B 191, 752-757 (hereinafter "Benson"). Claims 43 and 53 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Wallace et al. and Benson further in view of Hai et al., Bioconjugate Chem., 2000, 11, 705-713 (hereinafter "Hai et al."). Specifically, the Examiner asserts that the claimed method/hydrogel is an obvious design choice to one skilled in the art in view of the combined disclosure of the cited references.

Applicants respectfully submit that the claimed invention, as amended, is not rendered obvious by the cited references because the combined disclosures of the cited references do not teach or suggest the claimed limitations of the present invention. Furthermore, there is no disclosure or suggestion available in the cited references, or otherwise of the record, which would motivate one skilled in the art to modify the prior art methods in such a way to obtain the present invention.

Establishing prima facie obviousness requires a showing that the prior art references, when combined, teach or suggest all the claim limitations. Furthermore, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Recently, the United States Supreme Court also expressed the need to an "explicit" showing of "some apparent reason to combine the known elements in the fashion claimed by the patent at issue" and that "rejection on obviousness grounds cannot be sustained by mere

conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, slip op. at 14 (2007).

The claimed invention is directed to a method having the steps of priming the surface of a musculoskeletal tissue with a priming agent; adding a polymerizable agent and a radical photoinitiator to the primed musculoskeletal tissue; and reacting the primed musculoskeletal tissue with the polymerizable agent by a radical reaction. It is notable that the priming agent is bi-functional so as to be capable of reacting with both the musculoskeletal tissue and the polymerizable agent. More specifically, the priming agent contains at least one aldehyde group and at least one free radical polymerizable group, wherein the aldehyde group reacts with the musculoskeletal tissue to covalently bind the musculoskeletal tissue with the priming agent, and the free radical polymerizable group of the priming agent reacts with the free radical polymerizable group of the polymerizable agent to create a hydrogel covalently bound to the musculoskeletal tissue. Moreover, the free radical polymerizable groups are independently selected from the group consisting of an acrylate, diacrylate, oligoacrylate, methacrylate, dimethacrylate, and oligo methacrylate.

In contrast, neither of the two components of the Wallace composition are bi-functional. The polymerizable groups in the Wallace composition are either sulfhydryl groups or sulfhydryl-reactive groups which are in two separate components, respectively. Specifically, Wallace et al. disclose a method of forming a biocompatible gel which involves admixing component A having sulfhydryl groups and component B having sulfhydryl-reactive groups wherein the sulfhydryl-reactive groups can react with the sulfhydryl groups to form the gel. That is, the gel of Wallace et al. is formed via a crosslinking reaction between the sulfhydryl groups in component A and the sulfhydryl-reactive groups in component B.

Inasmuch as the gel formation is accomplished by crosslinking the sulfhydryl groups and the sulfhydryl-reactive groups in two separate components, Wallace et al. do not disclose or suggest a bi-functional component wherein one functional group reacts with the tissue and the other functional group crosslinks with the second component, as claimed by the present invention.

Furthermore, Wallace et al. fail to disclose or suggest replacing the sulfhydryl groups with any other free radical polymerizable groups, let alone a free radical polymerizable group selected from the group consisting of an acrylate, diacrylate, oligoacrylate, dimethacrylate, and oligo methacrylate.

Benson is a review article having 9 sections (sections 1 to 9). In general, Benson surveys the use of radiation in the biomaterials science (section 1). Specifically, Benson discloses the application of radiation in cardiovascular materials and devices (section 2), in pharmaceutical and scaffolding materials (section 3), in orthopedic materials (section 4), in bone and tissue adhesives (section 5), in dentistry (section 6), in sterilization (section 7), and in development of intelligent biomaterials (section 8). Thus, Benson summarizes that radiation induced crosslinking has allowed the tailoring of the composition and properties of hydrogels to meet numerous biomedical applications (section 9).

However, it is important to note that such a summary by Benson is based on the limited areas discussed in sections 1 to 8. Although Benson discloses the use of radiation in various biomaterials, it does not disclose or suggest the use of sulfhydryl groups in biomaterials, let alone replacing sulfhydryl groups with any other free radical polymerizable groups. Neither does Benson disclose or suggest a bi-functional component wherein one functional group reacts with the tissue and the other functional group crosslinks with the second component.

Therefore, the combined disclosures of Wallace et al. and Benson fail to disclose or suggest the claimed method of integrating a hydrogel to a musculoskeletal tissue.

Furthermore, Wallace et al. teach away from the present method because when the attachment of the tissue surface to another surface is needed, Wallace et al. prefer mixing all reactive components of the composition prior to delivery of the composition to a tissue surface (column 31, lines 4-21). It is true Wallace et al. generally disclose that the compositions may be delivered to the administration site in such a way that the individual components come into contact with each other for the first time at the administration site or immediately preceding administration (column 28, lines 3-7). However, when the method is for effecting the attachment of a tissue surface to another surface, as the priming agent does in the present invention, Wallace et al. specifically teach the following:

> "Preferably, all reactive components of the reactive composition are first mixed to initiate crosslinking, then delivered to the first surface before substantial crosslinking has occurred." (column 31, lines 14-17)

In contrast, in the present invention, when the musculoskeletal tissue forms a covalent attachment with the priming agent, the free radical polymerizable groups of the priming agent and the polymerizable agent are not first mixed to initiate crosslinking. Instead, the priming agent is applied to the musculoskeletal tissue to form a covalently bond prior to the application of the polymerizable agent. Thus, Wallace et al. teach away from the present invention.

Applicants respectfully submit that one skilled in the art, in view of the sulfhydryl-based crosslinking and the teaching away of Wallace et al. as well as the general summary of Benson without any specific suggestion, would not be motivated to devise a bi-functionalized component or replace the sulfhydryl groups of Wallace et al. with the claimed free radical polymerizable groups to arrive at the present invention.

In addition, Hai et al. do not cure the defects of the combined disclosures of Wallace et al. and Benson because Hai et al. disclose a method for preparing chondrotin-4-sulfate reagents and do not disclose or suggest replacing the sulfhydryl groups in biomaterials with the free radical polymerizable groups recited in the amended claims. Inasmuch as the principle references, namely, Wallace et al. and Benson, which spur each of the obviousness rejections, fail to teach or suggest the claimed limitations of the present invention, Hai et al. is further removed as is evidenced by including the reference in rejecting aspects of Applicants' dependent claims.

Therefore, the claimed invention, as amended, is not rendered obvious by the cited references.

Rejections under the Obviousness-type Double Patenting

Claims 40 to 59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 40 to 75 of copending Application No. 11/369,578. Claims 40 to 42, 45 to 48, 50 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 2, 9, 10, and 15 of copending Application No. 10/962,278 in view of Hai et al. Claims 40 to 42, 45 to 48, 50 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory

obviousness-type double patenting as allegedly unpatentable over claims 4 to 7, 18, 22, and 23 of copending Application No. 11/637,516 in view of Hai et al. Claims 40 to 42, 45 to 47, 49 to 52, and 55 to 58 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 53, 63, 65, 77, and 86 of copending Application No. 10/681,753 in view of Hai et al.

Applicants respectfully note the provisional obviousness-type double patenting rejections and will address these rejections when the Examiner find allowable subject matter in the present application.

Conclusion

In view of the foregoing, favorable reconsideration and allowance of the present application is respectfully solicited.

Except for issue fees payable under 37 C.F.R.§ 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R.§ 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. § 1.136(a)(3).

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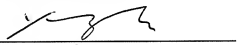
By: 

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